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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,176	07/12/2004	George A. Doherty	21014YP	7849

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
06/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,176	DOHERTY ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This Office Action is in response to the amendment submitted on 02/25/08. Claims 6-11 are currently pending in the application, with claims 1-5 and 12-61 having being cancelled. Accordingly, claims 6-11 are being examined on the merits herein.

Receipt of the aforementioned amended claims and abstract is acknowledged and has been entered. Moreover, in view of applicant's amendment of the claims, the lack of written description rejection under 35 U.S.C. § 112, first paragraph and lack of antecedent basis rejection are withdrawn.

Applicant's argument with respect to the scope of enablement rejection has been fully considered but is not found persuasive. While Examiner appreciates applicant's contention that the compounds of the invention are not for the treatment of lymphopenia but rather its induction, Examiner respectfully points out that the scope of enablement rejection was directed to the aforementioned compounds in the treatment of all immunoregulatory abnormalities. Given that applicant failed to provide any support that all the aforementioned compounds are helpful in the treatment of any immunoregulatory abnormality and given that applicant equally failed to provide support that the aforementioned compounds are helpful in the treatment of all immunoregulatory

abnormalities, the scope of enablement rejection is deemed proper. Additionally, applicant's arguments that the data from Hale et al. provides support for the aforementioned compounds is unpersuasive given that the reference possesses a 2004 publication date which is well after applicant's claim for priority (i.e. 01/18/02). Moreover, this further suggests that applicant was not in possession of the aforementioned claims as of the claimed priority date.

For the foregoing reasons, the rejection of claims 1-11, 13-14, 19, and 46-59 under 35 U.S.C. § 112, first paragraph and the ODP rejections of claim 1 remain proper and are maintained. In view of applicant's amendment, the following modified 112, first paragraph Final rejections are being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

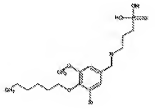
In this application, applicant claims that the compounds of the invention listed in the specification on pgs. 13-27 possess at least 100, 200, 500, 1000, or 2000-fold selectivity for the S1P1 receptor over S1P3 receptor, yet applicant provides no support for the claimed compounds. In fact, applicant solely provided one example of a compound (i.e. example 77 that contains an alkyl chain near the phosphate group) that is structurally different from the aforementioned azetidine or pyrrolidine-containing compounds. Consequently, due to this lack of written description, the exact selectivity of the aforementioned compounds being claimed by applicant to be used in their method cannot be fully ascertained.

Scope of Enablement Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for



(i.e. example 77) in the suppression of the immune system, does not reasonably provide enablement for all of the disclosed compounds in the specification (see pages 13-27) in the suppression of the immune system. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of suppressing the immune system in a mammalian patient in need of such immunosuppression comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective suppressing the immune system, wherein said compound possesses a selectivity for the over S1P1/Edg1 receptor over S1P3/Edg3 receptor. The instant specification fails to provide information that would allow the skilled artisan to practice the suppression of the immune system with all of the aforementioned compounds.

In re Sichert, 196 USPQ 209 (CCPA 1977)

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

The test is not merely quantitative, since a considerable amount of experimentation is

> permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The invention relates to a method of suppressing the immune system in a mammalian patient in need of such immunosuppression comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective suppressing the immune system, wherein said compound possesses a selectivity for the over S1P1/Edg1 receptor over S1P3/Edg3 receptor. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. For example, Examiner cites the fact that the compounds of the invention are structurally different and therefore it is highly unlikely to predict that all of the aforementioned compounds would behave similarly.

2. The breadth of the claims

The claims are thus very broad insofar as they recite the "suppression of the immune system" with all of the aforementioned compounds. While such "suppression" might theoretically be possible for some of the aforementioned compounds, as a practical matter it is rather unpredictable to conclude that all of the aforementioned compounds would suppress the immune system without undue experimentation.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for any of the aforementioned compounds in the suppression of the immune system. In fact, other than example 77, a compound structurally different from the claimed compounds, applicant provides no support for the aforementioned claims. While the instant disclosure suggests that this

unique activity can be extrapolated to the aforementioned compounds, the fact that example 77 is structurally different from the aforementioned compounds suggest undue experimentation for identifying their selectivities for the S1P1 receptor over the S1P3 receptor, and thus does not meet the "how to use" prong of 35 USC 112, first paragraph with regard thereto.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed compounds could be predictably used for the suppression of the immune system as inferred by the claims and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

06/17/08

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617